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(54) Title: PROCESS FOR PREPARING PURE CEPHALOSPORINS INTERMEDIATES

(57) Abstract: The present invention relates to a process for preparing key intermediates for cephalosporin antibiotics substantially free of undesired delta A² isomer. Thus, 7-aminocephalosporanic acid (7-ACA) is silylated with hexamethyldisilazane in cyclohexane at reflux temperature. (6R,7R)-3-[(Acetyloxy)methyl]-7-(trimethylsilyl)aminoceph-3-em-4-oic acid obtained is reacted with the mixture of N-methylpyrrolidine and trimethylsilyliodide in cyclohexane, desilylated with isopropyl alcohol and treated with hydrochloric acid to obtain [6R-(6a,7b)]-1-[[[7-Amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-1-methylpyrrolidinium inner salt hydrochloride. [6R-(6a,7b)]-1-[[[7-Amino-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-1-methylpyrrolidinium inner salt hydrochloride is N-acylated with syn-2-(2-aminothiazol-4-yl)-2-methoxyimino acetic acid 2-benzothiazolyl thioester (MAEM) followed by treatment with hydrochloric acid to give cefepime dihydrochloride monohydrate.



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